Electronic Supplementary Material (ESI) for Chemical Communications.

Supplementary Material

Disentangling scalar coupling patterns by real-time SERF NMR

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Experimental

Cyclo-Phe-Pro was obtained from Bachem AG (Bubendorf, Switzerland). All other chemicals were purchased from by Sigma-Aldrich (St. Louis, MO, USA) at > 98% purity. All experiments were carried out on a Bruker AVANCE III 500 MHz spectrometer using a 5 mm TXI probe with z-axis gradients at 298 K.

One-dimension real-time SERF spectra were obtained using a 60 ms EBURP-2 pulse for slice-selective excitation during a weak pulsed field gradient of 1.5 G/cm. During the interrupted acquisition we used 10-15 ms 180° Gaussian pulses for refocusing and two 270° Gaussian pulses of 10 ms each, for selective recoupling. A total of 80 individual FID data chunks of 25 ms were added up automatically during acquisition, resulting in a total acquisition time of ~ 2 s.

Computational details

Starting from the X-ray structure of cyclo-Phe-Pro (CITXAE12 [1,2]) a conformational search using the mixed torsion/low-frequency-mode Monte Carlo sampling with $CHCl_3$ as the solvent, as implemented in Maestro [3] in combination with the OPLS 2005 force field [4] was performed. The resulting 5 unique conformations within an 5 kcal mol^{-1} window were then re-optimized with the dispersion-corrected B97D density functional [5] and the 6-31G(d,p) basis set using Gaussian 09 [6]. Solvent effects (DMSO) were approximated using the SMD solvation model [6]. All structures were characterized by frequency calculations and thermochemical data were obtained by the standard rigid-rotor harmonic-oscillator approximation. Final relative Gibbs free energies used for Boltzmann-weighting are based on LPNO-CEPA/1 calculations [7-10] using the def2-TZVPP [11,12] basis set combined with B97D/6-31G(d,p) thermal corrections based on Grimme's quasi-RRHO approach [13] to estimate entropic contributions from low-frequency vibrations ($\nu < 100$ cm^{-1}; $\alpha = 4$ and $B_{av} = 10^{-44}$ kgm^{-1}). Finally, SMD-B97D/6-31G(d,p) solvation (DMSO) energies were added. NMR coupling constants were calculated using the pcJ-2 basis set [14] and weighted by the Boltzmann factor of the individual conformations. Programs used were Gaussian 09 [15] and ORCA [16,17].

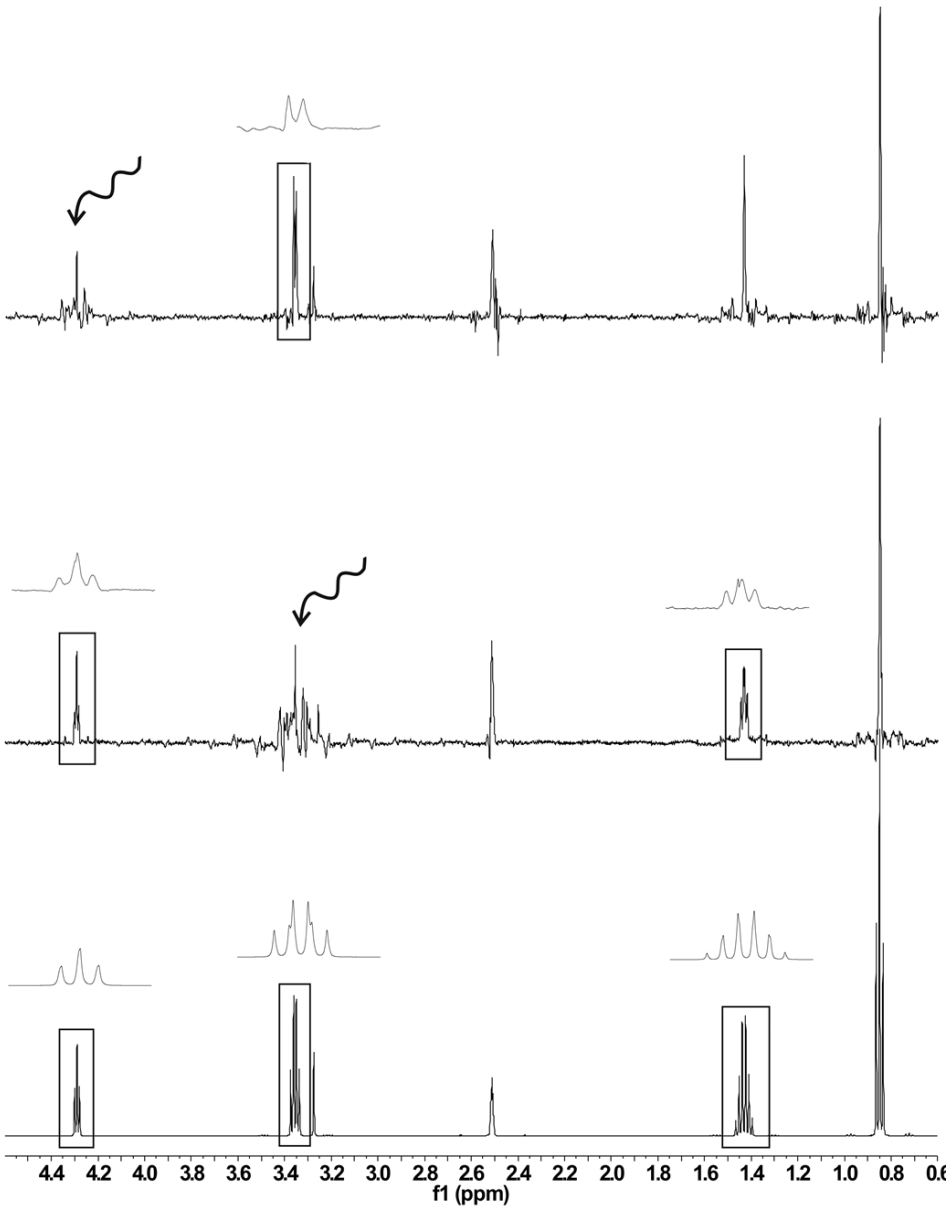

Figure S1: A regular 1D ^{1}H spectrum (bottom) and two single scan real-time SERF spectra of a solution of 8 mg n-propanol in 600 µl DMSO-d_6, recorded at 310 K on a Bruker Avance III 500 MHz NMR spectrometer without cryo probe. The selectively refocused signals are indicated by the wavy arrows.

Supporting References

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Pulse-sequence of the real-time SERF experiment:

```
;avance-version
;1D sequence with explicit programming of acquisition
;
;$CLASS=HighRes
;$DIM=1D
;$TYPE=
;$SUBTYPE=
;$COMMENT=


#include <Avance.incl>
#include <De.incl>
#include <Grad.incl>
#include <Delay.incl>

dwellmode explicit



"d11=3u"
"d12=6.5u"
"d20=10u"
"d2=aq/l0"
"d3=d2/2"
"l1=l0-1"
"p2=2*p1"


1 ze
2 3m
  4u BLKGRAD
  d1 rpp2
  50u UNBLKGRAD

  d12 pl0:f1
  d12 gron1
  (p12:sp12 ph1)
  d12 groff
  d12 pl1:f1



  ACQ_START(ph30,ph31)

   0.05u DWL_CLK_ON
   0.1u REC_UNBLK
   d3:r
   0.1u REC_BLK
   0.05u DWL_CLK_OFF

   p16:gp2

   d16 pl0:f1
   10u
   (p24:sp24 ph14)
```

```
   10u

   d16 pl1:f1
   p2 ph2

   d16 pl0:f1
   10u
   (p24:sp24 ph14)
   10u

   p16:gp3
   d16

   1m
   d16 pl0:f1
   10u
   d11 gron1
   (p13:sp13 ph3)
   d11 groff
   10u
   p16:gp4
   d16

3  0.05u DWL_CLK_ON
   0.1u REC_UNBLK
   d2:r
   0.1u REC_BLK
   0.05u DWL_CLK_OFF

   p16:gp2

   d16 pl0:f1
   10u
   (p24:sp24 ph14)
   10u

   d16 pl1:f1
   p2 ph2

   d16 pl0:f1
   10u
   (p24:sp24 ph14)
   10u

   p16:gp3
   d16

   1m
   d16 pl0:f1
   10u
   d11 gron1
   (p13:sp13 ph3)
   d11 groff
   10u
   p16:gp4
   d16

lo to 3 times l1
```

```
  0.05u DWL_CLK_ON
   0.1u REC_UNBLK
   d3:r
   25m
   0.1u REC_BLK
   0.05u DWL_CLK_OFF


rcyc=2


wr #0

exit

;ph1  = 0
;ph2  = 0
;ph31 = 0
;ph30 = 0
ph1 =0 2 2 0 1 3 3 1
ph2 = 0 2
ph3 = 2 0
ph14 = 0 0 2 2
ph30=0
ph31=0 2 2 0 1 3 3 1


;pl1 : f1 channel - power level for pulse (default)
;p1 : f1 channel -  high power pulse
;d1 : relaxation delay; 1-5 * T1
;d7 : Serf delay
;NS: 1 * n, total number of scans: NS * TD0
;l20:


;$Id: zgadc,v 1.12 2009/07/02 16:40:47 ber Exp $
```